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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,164	04/04/2005	Susanne Binder	34157-707.831	5602

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EXAMINER	
KIM, TAEYOON	
ART UNIT	PAPER NUMBER
1651	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,164	BINDER ET AL.	
	Examiner	Art Unit	
	Taeyoon Kim	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42,43,45-49 and 53-61* is/are pending in the application.

4a) Of the above claim(s) *60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42,43,45-49,53-59 and 61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Applicant's amendment and response filed on Aug. 28, 2007 has been received and entered into the case.

Claims 1-41, 44 and 50-52 are canceled, claim 60 is withdrawn from consideration as being drawn to non-elected subject matter, and claims 42, 43, 45-49, 53-59 and 61 have been considered on the merits. All arguments have been fully considered.

The claim objection in the previous office action is withdrawn due to the amendment.

The claim rejections under 35 U.S.C.§112 are withdrawn due to the amendment.

Response to Arguments

Applicant's arguments filed 8/28/07 have been fully considered but they are not persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant argued that Liu does not teach or suggest a composite comprising amniotic membrane and a RPE cells or RPE equivalent cells, and such composite capable for treating a retinal disease. In the previous office action, it is clearly disclosed

that Liu does not teach the amniotic membrane and the teaching of Dutt et al., using an amniotic membrane as a substrate for culturing pigment epithelial cell (RPE).

Applicant argued that Dutt et al. do not describe any therapeutic applications. It is not relevant whether or not the method or product of Dutt et al. is for treating a retinal disease. The teaching of Dutt et al. combined with the method of Liu is the use of amniotic membrane, as a substrate for RPE cells, not the whole teaching of Dutt et al.

Thus, the holding of obviousness rejections are required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 42, 43, 45-46, 49, 54, 57-59 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu (US 6,045,791; IDS reference #7) in view of Dutt et al.

(1991; IDS ref. #15).

Claims 42, 43, 45-46, 49, 54, 57-59 and 61 are drawn to a method for treating a retinal disease, comprising inserting a composite comprising amniotic membrane and retinal pigment epithelial cells in a subretinal space of a patient in need thereof (claim 42); a limitation to the epithelial cells being from about 16,000 to about 20,000 per 4 mm^2 of the amniotic membrane (claim 43); a limitation to the retinal disease being age-related macular degeneration (claim 45); a limitation to the amniotic membrane being human (claim 46); a limitation to the retinal pigment epithelial cells being cultured on the amniotic membrane (claim 47); a limitation to the amniotic membrane comprising a basement membrane and a stroma (claim 54); a limitation to the amniotic membrane being treated on one side with excimer laser ablation (claim 57); a limitation to the excimer laser ablation altering the thickness of the stromal side or basement membrane of the amniotic membrane (claim 58); a limitation to the retinal pigment epithelial equivalent cells being iris pigment epithelial cells, retinal pigment epithelial cells differentiated from an adult or embryonic stem cell, cells derived from neural retinal cells or cell derived from a ciliary body (claim 59); a limitation to the composite being formed by applying retinal pigment epithelial cell or its equivalent to an amniotic membrane, and culturing the cells on the membrane under the condition for growth (claim 61).

Liu teaches a method of treating a retinal disorder such as age-related macular degeneration, by transplanting retinal pigment epithelium (RPE) cells cultured on an attachment substrate into the subretinal area of a patient in need thereof (see Abstract and column 7, lines 57-59 and 65-67; Example 1).

Liu does not teach the use of amniotic membrane.

Dutt et al. teach the use of human amniotic membrane as a substrate for culturing retinal pigment epithelial cells (see whole document).

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to replace the collagen substrate of Liu with the amniotic membrane of Dutt et al. in the method of Liu.

The skilled artisan would have been motivated to make such a modification because both the substrate of Liu and the amniotic membrane of Dutt et al. are used for the growing RPE cells, they are considered as art-recognized equivalents for growing RPE cells for transplantation.

M.P.E.P. §2144.06 states "In re Scott, 323 F.2d 1016, 139 USPQ 297 (CCPA 1963) (Claims were drawn to a hollow fiberglass shaft for archery and a process for the production thereof where the shaft differed from the prior art in the use of a paper tube as the core of the shaft as compared with the light wood or hardened foamed resin core of the prior art. The Board found the claimed invention would have been obvious, reasoning that the prior art foam core is the functional and mechanical equivalent of the claimed paper core. The court reversed, holding that components which are functionally or mechanically equivalent are not necessarily obvious in view of one another, and in this case, the use of a light wood or hardened foam resin core does not fairly suggest the use of a paper core.); Smith v. Hayashi, 209 USPQ 754 (Bd. of Pat. Inter. 1980) (The mere fact that phthalocyanine and selenium function as equivalent photoconductors in the claimed environment was not sufficient to establish that one

would have been obvious over the other. However, there was evidence that both phthalocyanine and selenium were known photoconductors in the art of electrophotography. "This, in our view, presents strong evidence of obviousness in substituting one for the other in an electrophotographic environment as a photoconductor." 209 USPQ at 759.)."

Although Liu in view of Dutt et al. do not particularly teach the number of cells on the amniotic membrane, however, because the number of cells used in the claimed method is considered as one of result effective variables. As such, the variables would be routinely optimized by one of ordinary skill in the art in practicing the invention disclosed by those references. Generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed atl a temperature of 100°C and an acid concentration of 10%.); >see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); ** In re Hoeschele, 406 F.2d 1403, 160 USPQ 809

(CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the :references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). Accordingly, the claimed invention was prima facie obvious to one of ordinary skill in the art at the time the invention was made especially in the absence of evidence to the contrary.

Although Liu in view of Dutt et al. do not particularly disclose the presence of "pharmaceutically active molecule" in the method, since it is well known in the art that the amniotic membrane contains various growth factors, the limitation of "pharmaceutically active molecule" is inherently accomplished by the use of amniotic membrane. Since Dutt et al. disclose a culture condition of human pigment epithelial cells on the amniotic membrane using culture medium containing growth factors, enzymes and therapeutic drugs, the method of Liu in view of Dutt et al. would contain a composite comprising amniotic membrane and RPE cells with other growth factors, enzymes and/or therapeutic drugs because of culturing condition of the RPE cells.

Although Liu in view of Dutt et al. do not particularly teach the use of excimer laser ablation technique, since it is necessary to cut the substrate, having RPE cells grown on it, for transplantation as described in Liu (see Example 1, column 11, lines 10-11), and excimer laser ablation technique is well known in the art to cut and reshape

variety of tissues, it would have been obvious for a person of ordinary skill in the art to optimize the cutting procedure by using a technique with high precision such as excimer laser ablation technique. Further, a surgical instrument used in the method of Liu for cutting the substrate containing RPE cells and excimer laser ablation would be considered as art-recognized equivalents, and therefore, the excimer laser ablation would be used in place of the surgical instrument for cutting the substrate for transplantation.

The limitation of claim 58 is considered as a result of the method step in claim 57. Claim 58 contains a "wherein" clause that merely states the result of the limitations in the claim and therefore, adds nothing to the patentability or substance of the claim. Therefore, this phrase does not limit the claim. See *Texas Instruments Inc. v. International Trade Commission*, 26 USPQ2d 1010 (Fed. Cir. 1993); *Griffin v. Bertina*, 62 USPQ2d 1431 (Fed. Cir. 2002); *Amazon.com Inc. v. Barnesandnoble.com Inc.*, 57 USPQ2d 1747 (Fed. Cir. 2001).

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Claims 48 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu (supra) in view of Dutt et al. (supra), in further view of Dua et al. (1999; IDS ref. #19).

Claims 48 and 49 are drawn to a limitation to the composite further comprising a pharmaceutically active molecule (claim 48); a limitation to the pharmaceutically active

molecule being growth factors, enzymes, or therapeutic drugs (claim 49).

Liu in view of Dutt et al. render the subject matter of claim 42 obvious (see above).

Although Liu in view of Dutt et al. do not teach the presence of "pharmaceutically active molecule" in the composite of the method, the limitation of "pharmaceutically active molecule" is inherently accomplished by the use of amniotic membrane of Dutt et al. in the method of Liu. Because Dutt et al. teach the amniotic membrane produces various growth factors such fibroblast growth factor (see p.748, right column, a section under the title of "Amniotic membrane in ophthalmology").

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Claim 53 is rejected under 35 U.S.C. 103(a) as being unpatentable over Liu (supra) in view of Dutt et al. (supra), in further view of Grueterich et al. (2002; IDS ref. #28).

Claim 53 is drawn to a limitation to the amniotic membrane being epithelially denuded.

Liu in view of Dutt et al. render the subject matter of claim 42 obvious (see above).

Liu in view of Dutt et al. do not teach the amniotic membrane being epithelially denuded.

Grueterich et al. teach the use of epithelially denuded amniotic membrane in

culturing limbal epithelium (see whole document; p.64, Materials and Method).

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to use epithelially denuded amniotic membrane of Grueterich et al. in the method of Liu in view of Dutt et al.

The skilled artisan would have been motivated to make such a modification because both intact and epithelially denuded amniotic membrane would be suitable for support of epithelial cell culture. Since amniotic membrane is a suitable substrate for culturing not only corneal epithelial cells as taught by Grueterich et al. but also for RPE cells, a person of ordinary skill in the art would have considered the choice of intact or denuded amniotic membrane as a routine optimization procedure to obtain optimal environment for culturing RPE cells for treating a retinal disorder.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Claims 55 and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu (supra) in view of Dutt et al. (supra), in further view of Tseng (US 6,152,142; IDS ref. #1).

Claims 55 and 56 are drawn to a limitation to the method further comprising a step of adding mesenchymal cells to one side of the stroma (claim 55); a limitation to the mesenchymal cells being fibroblasts (claim 56);

Liu in view of Dutt et al. render the subject matter of claim 42 obvious (see above).

Liu in view of Dutt et al. do not teach a step of adding mesenchymal cells to the stroma of the amniotic membrane or the mesenchymal cells being fibroblasts.

Tseng teaches that when fibroblasts (mesenchymal cells) are grown in the stromal side of amniotic membrane, it provides an environment comparable to isolated collagen (fibroblasts are collagen-producing cells) and better cell growth in culture than a plain plastic surface.

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to add fibroblasts on the stromal side of the amniotic membrane of Liu in view of Dutt et al.

The skilled artisan would have been motivated to make such a modification because Tseng teaches an advantage given by the fibroblast culture on the stromal side of the amniotic membrane providing better cell culture environment for epithelial cells.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taeyoon Kim whose telephone number is 571-272-9041. The examiner can normally be reached on 9:00 am - 5:00 pm ET (Mon-Thu).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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